Docket No. 04674.105074 (TRI 1016)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s):	Philip A. Furman	Confirmation:	6903
Serial No.:	10/618,531	Group Art Unit:	1614
Filed:	July 11, 2003	Examiner:	Donna Jagoe

For: Combination Therapies with L-FMAU for the Treatment of Hepatitis B Virus Infection

ATTACHMENT TO FORM PTO/SB/33:

PRE-APPEAL BRIEF REQUEST FOR REVIEW

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

The following remarks are made as an attachment to Form PTO/SB/33 to provide reasons for the requested review. Applicants request a review of the record, including the final rejection dated August 4, 2009. Applicants assert that a review of the record will show that the finality of the Office Action dated August 4, 2009 should be withdrawn, the pending claims should be found patentable over the cited references, and the application should be passed to issue.

A listing of the pending claims can be found on pages 2-3 of the response filed on March 30, 2009. Claims 1-8 are rejected under 35 U.S.C. § 103(a) as being unpatentable in view of Schinazi et al. (U.S. Patent No. 5,703,058) and Thyagarajan (U.S. Patent No. 6,589,570).

In the Office Action dated August 4, 2009, the basis for the rejection under 35 U.S.C. § 103(a) from page 2, line 12 through page 5, line 17 is essentially identical to the arguments presented in the Office Action (non-final rejection) dated September 30, 2008. In response, Applicants rely on the arguments presented in the response filed March 30, 2009. Specifically, Applicants rely on the following arguments:

1) the Office Action fails to meet the legal standard for obviousness (see page 5, line 7, through page 7, line 3, of the response filed March 30, 2009);

2) the Office Action mischaracterizes the teachings of the cited art (see page 7, line 4, through page 10, line 8, of the response filed March 30, 2009);

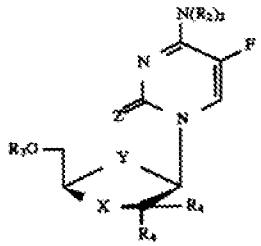
3) the Office Action fails to provide motivation for administration of three components (see page 10, line 9, through page 11, line 2, of the response filed March 30, 2009);

4) the cited references fail to provide a reasonable expectation of success (see page 11, line 3, through page 12, line 11).

With regard to the "Response to Arguments" section on page 5, line 18, through page 9, line 2, of the Office Action (final rejection) dated August 4, 2009, Applicants submit the following additional comments:

I. The Office Action continues to mischaracterize Schinazi (U.S. Patent No. 5,703,058)

The Office Action relies on the structure at col. 3, lines 31-44, from Schinazi:



and argues that because one can select the variables R_2, R_3, R_4, X, Y, and Z with the benefit of hindsight to arrive at L-(-)-FTC from among thousands if not millions of possible compounds, therefore "[t]his structure is Emtricitabine (aka FTC)." (OA, p. 7, line 11). Applicants respectfully submit that Schinazi's teaching of a genus of thousands or millions of possible compounds lacks the specificity asserted by the Examiner, and to assert that Schinazi teaches the specific compound is a mischaracterization of the teachings of Schinazi. Absent hindsight reconstruction of Applicant's own disclosure, arriving at L-(-)-FTC in the claimed combination

from the genus of Schinazi is less likely than finding a needle in a haystack or arriving at the combination of a padlock with the knowledge that each number ranges from 0 to 9.

II. The Office Action continues to mischaracterize Thyagarajan (U.S. Patent No. 6,589,570)

The Office Action relies on the following passage from Thyagarajan:

eliminate HBV carrier status. Research conducted from the mid 70s have delineated several agents to have treatment potential in chronic HBV infections which has been illustrated in the Table 1 given below.

TABLE 1

Agents that have been studied in the treatment of HBV infection (Lau et al., Gut, Suppl. 1991;547-562)

Anti-virals	Immunosuppressive	Immunostimulators
Interferons	Corticosteroids	BCG vaccination
Alpha interferon		Levamisole
Beta interferon		Interleukin-2
Gamma interferon		Interferon gamma
Tumour necrosis factor		Thymosin
Adenine arabinoside (Ara-A)		Tumor necrosis
Acyclovir, deoxyacyclovir		factor
Zidovudine		
Suramin		
Ribavirin		
Phosphonoformate		
Quinacrine		
(+) -cyanidanol-3		
Lamuvidine		
Phyllanthus amarus		

However, except the interferons, Lamuvidine and the latest entry *Phyllanthus amarus*, the others seem to be far from successful. The limited success rate, prohibitive cost, profound side effects and the non-accessibility of interferons and Lamuvidine in developing and underdeveloped counties have necessitated further search for newer antihepatitis B agents.

(Thyagarajan, col. 2, lines 16-46). The Office Action states

> the limit on the success cited by Thyagarajan is because of prohibitive costs, side effects and limited accessibility. These limitations are not statements that the interferon is not effective in treating hepatitis B; it is a statement of the accessibility of the interferon. It does not teach away from the use of interferon.

(OA, p. 8, lines 7-10). Applicants respectfully disagree, and note that Thyagarajan specifically recites four deficiencies with interferon: 1) limited (i.e., poor) success rate; 2) prohibitive cost; 3) profound side effects; and 4) non-accessibility. Rather than teaching one of ordinary skill in the art to use interferon, Thyagarajan summarizes the deficiencies of interferon and specifically

teaches one of ordinary skill in the art to "search for newer antihepatitis B agents." This is an explicit teaching away, and it is improper for the Office Action to ignore this explicit teaching from the cited art.

III. There is a clear legal deficiency in the Office Action because it fails to meet the standard of obviousness

The legal standard for obviousness is discussed in previous responses. See, for example, the Response filed March 30, 2009. The Office Action fails to provide a reasonable expectation of success in combining the three active agents according to the claims. Where one of ordinary skill in the art would be guided by both experience and theory, the Office Action suggests an improper try-anything approach from thousands if not millions of compounds in order to retroactively arrive at Applicants' own invention. This fails to properly consider the fact that the cited art (Thyagarajan) teaches away from the present invention and fails to provide any specificity (Schinazi).

Applicants note that the references relied upon by the Office Action provide no data that one of ordinary skill in the art could evaluate with regard to antihepatitis B efficacy for the triple-combination. Therefore, the rejection clearly fails to make a prima facie case of obviousness. Moreover, Applicants have provided evidence from the literature (see Osborn) that actual combinations when tested are inferior to monotherapy (p. 1033, left column, lines 34-36), and that "the promise of combination therapy remains elusive for hepatitis B" (p. 1033, left column, lines 36-37).

IV. There is a clear legal deficiency in the Office Action in that the Office Action improperly ignores the Osborn reference

The Office Action states that

> Applicant's reliance on the post filing date reference, Osborn (April 2006), to allegedly provide evidence of non-obviousness is not persuasive. The determination of obviousness or non-obviousness must be based upon what was known in the art at the time the invention was made. See 35 U.S.C. § 103

(OA, p. 8, lines 17-21). The Examiner's refusal to consider the evidence in Osborn is in direct contradiction to the policy set forth in the MPEP:

> References which do not qualify as prior art because they postdate the claimed invention may be relied upon to show the level of ordinary skill in the art at or around the time the invention was made. *Ex parte Erlich*, 22 USPQ 1463 (Bd. Pat. App. & Inter. 1992).

(MPEP 2124). Osborn provides evidence that one of ordinary skill in the art at the time of the invention would not have an expectation of success in randomly combining antihepatitis B agents. Applicants are entitled to the consideration of the evidence in Osborn of actual failure of attempts to combine antihepatitis B agents, and that evidence of such failure rebuts the Examiner's unsupported assertion of a reasonable expectation of success.

In view of the clear legal and factual deficiencies in the Office Action of August 4, 2009, Applicants respectfully request withdrawal of the finality of the Office Action and allowance of the claims over the cited references.

The Commissioner is hereby authorized to charge any fees which may be required for consideration of this submission to Deposit Account No. **50-3732**, Order No. 04674-105074.

Respectfully submitted,
King & Spalding, LLP

Dated: February 4, 2010

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PTO/SB/33 (07-09)
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PRE-APPEAL BRIEF REQUEST FOR REVIEW

Docket Number (Optional): 04674.105074

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on _____

Signature _____

Typed or printed name _____

Application Number	Filed
10/618,531	July 11, 2003

First Named Inventor: Philip A. Furman

Art Unit	Examiner
1619	Donna A. Jagoe

Applicant requests review of the final rejection in the above-identified application. No amendments are being filed with this request.

This request is being filed with a notice of appeal.

The review is requested for the reason(s) stated on the attached sheet(s).
Note: No more than five (5) pages may be provided.

I am the

- ☐ applicant/inventor.
- ☐ assignee of record of the entire interest. See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed. (Form PTO/SB/96)
- ☑ attorney or agent of record. Registration number 53,913.
- ☐ attorney or agent acting under 37 CFR 1.34. Registration number if acting under 37 CFR 1.34 _____

/michael willis/
Signature

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Telephone number

February 4, 2010
Date

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below*.

☐ *Total of _____ forms are submitted.

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